



## **ADMA: an emerging cardiovascular risk factor**

Rainer H Böger, John P Cooke, Patrick Vallance

### **► To cite this version:**

Rainer H Böger, John P Cooke, Patrick Vallance. ADMA: an emerging cardiovascular risk factor. *Vascular Medicine*, 2005, 10 (2), pp.S1-S2. <10.1191/1358863x05vm594ed>. <hal-00572115>

**HAL Id: hal-00572115**

**<https://hal.science/hal-00572115v1>**

Submitted on 1 Mar 2011

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

# Editorial

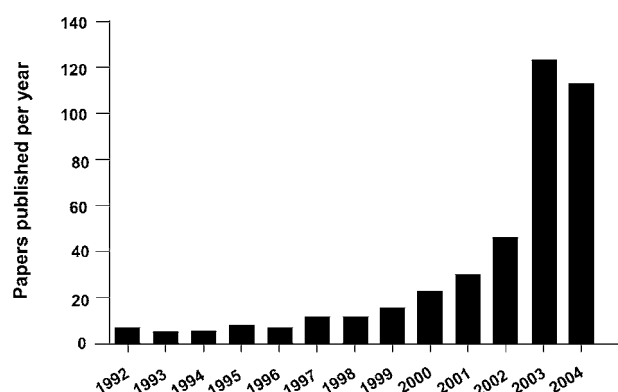
## ADMA: an emerging cardiovascular risk factor

Rainer H Böger<sup>a</sup>, John P Cooke<sup>b</sup> and Patrick Vallance<sup>c</sup> (guest editors)

Two years have passed since we first gathered together researchers from around the world to exchange their thoughts and data. Since that meeting in Hamburg, Germany, the evidence has grown that ADMA plays a significant role in cardiovascular physiology and pathology. The rapid growth of the field compelled a second meeting, held in New Orleans in November 2004. This issue of *Vascular Medicine* contains the proceedings from that meeting, at which new and exciting data emerged, of scientific interest and clinical relevance.

ADMA is asymmetric dimethylarginine, an endogenous inhibitor of nitric oxide (NO) synthase. ADMA has been recognized as a metabolite since the 1970s, but its functional role as a competitive inhibitor of NO synthase was first described by one of us (PV) in 1992.<sup>1</sup> Although the importance of this molecule was immediately apparent to endothelial biologists, ADMA did not attract the attention of the general scientific and clinical community until recently. Cardiologists, nephrologists, pharmacologists and others are currently among those who are actively pursuing research on ADMA. This is witnessed by the rapidly increasing number of scientific publications on the topic (the numeric results of a recent MEDLINE search are displayed in Figure 1). We anticipate a surge in interest from clinical investigators now that the scientific foundation has been laid, and now there are high throughput technologies for measurement of ADMA.

In October 2002, first attempts were made to understand the biosynthesis and metabolism of ADMA as



**Figure 1** Numeric results of a MEDLINE search dated 19 January 2005, which included the search terms 'ADMA' and 'asymmetric dimethylarginine'.

well as some of its biological effects in the cardiovascular system. During our discussions at the first meeting in 2002 it became clear that an effort was needed to standardize analytical methods to measure ADMA because data generated by different groups of researchers and by different methods varied widely. At that time, the first studies had been published, which showed a relationship between ADMA and cardiovascular endpoints in controlled clinical trials.<sup>2–4</sup>

By November 2004, the role of ADMA as an emerging cardiovascular risk factor had been much more firmly established by multiple studies in different patient populations. The physiological importance of ADMA has been strongly supported by observations made using the DDAH transgenic mouse.<sup>5</sup> Early results from a DDAH knockout mouse appear to be consistent with the role of ADMA as a negative regulator of NO synthase. The mechanisms by which ADMA becomes elevated in patients with cardiovascular disease have been elucidated (for recent reviews see Böger 2003,<sup>6</sup> Cooke 2004,<sup>7</sup> Vallance and Leiper 2004<sup>8</sup>). Several therapeutic agents have been shown to reduce plasma ADMA levels in patients and those with risk factors, including angiotensin converting

<sup>a</sup>Clinical Pharmacology Unit, Institute of Experimental and Clinical Pharmacology and Toxicology, University Hospital Hamburg-Eppendorf, Germany; <sup>b</sup>Section of Vascular Medicine, Falk Cardiovascular Research Center, Stanford University School of Medicine, Stanford, CA, USA; <sup>c</sup>Centre for Clinical Pharmacology, The British Heart Foundation Laboratories, University College London, UK

Address for correspondence: Rainer H Böger, Clinical Pharmacology Unit, Institute of Experimental and Clinical Pharmacology and Toxicology, University Hospital Hamburg-Eppendorf, Germany. E-mail: boeger@uke.uni-hamburg.de

enzyme inhibitors, angiotensin receptor antagonists, and insulin sensitizing agents (metformin and rosiglitazone). However, we are still lacking specific interventions to reduce plasma ADMA.

All of these new data, as they were presented during the Second International Symposium on ADMA – an Emerging Cardiovascular Risk Factor, are condensed into this supplemental issue to *Vascular Medicine*. This supplement provides a comprehensive overview on ADMA for researchers and clinicians alike who are interested in this emerging field of vascular biology and medicine.

Certainly, there are still open questions: What are the exact levels of ADMA in various tissues? Which isoform of DDAH contributes to its metabolism in various diseases? Is ADMA a widely applicable disease marker useful for primary prevention in patients with severe disease? Large prospective clinical trials will be needed to answer these questions; however, we feel that the stage is set to do so, and we anticipate that we will have more answers to these questions when we reconvene in London in 2006.

## References

- 1 Vallance P, Leone A, Calver A, Collier J, Moncada S. Accumulation of an endogenous inhibitor of NO synthesis in chronic renal failure. *Lancet* 1992; **339**: 572–75.
- 2 Miyazaki H, Matsuoka H, Cooke JP. Endogenous nitric oxide synthase inhibitor: a novel marker of atherosclerosis. *Circulation* 1999; **99**: 1141–46.
- 3 Zoccali C, Bode-Böger SM, Mallamaci F et al. Asymmetric dimethylarginine (ADMA): an endogenous inhibitor of nitric oxide synthase predicts mortality in end-stage renal disease (ESRD). *Lancet* 2001; **358**: 2113–17.
- 4 Valkonen VP, Päivä H, Salonen JT et al. Risk of acute coronary events and serum concentration of asymmetrical dimethylarginine. *Lancet* 2001; **358**: 2127–28.
- 5 Dayoub H, Achan V, Adimoolam S et al. Dimethylarginine dimethylaminohydrolase regulates nitric oxide synthesis: genetic and physiological evidence. *Circulation* 2003; **108**: 3042–47.
- 6 Böger RH. The emerging role of ADMA as a novel cardiovascular risk factor. *Cardiovasc Res* 2003; **59**: 824–33.
- 7 Cooke JP. Asymmetrical dimethylarginine: the Über marker? *Circulation* 2004; **109**: 1813–18.
- 8 Vallance P, Leiper J. Cardiovascular biology of the asymmetric dimethylarginine:dimethylarginine dimethylaminohydrolase pathway. *Arterioscler Thromb Vasc Biol* 2004; **24**: 1023–30.